

Single center experiences in merkel cell carcinoma and unprecedented presentation

Single center experiences in merkel cell carcinoma

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Abstract

Aim: Merkel cell carcinoma (MCC) is a rare skin tumor with an aggressive course. If there is no distant metastasis in its treatment, excision with negative surgical margins is the primary method. Since it is usually detected in incidental postoperative pathology reports, negative surgical margins must be observed during the removal of lesions on the skin.

Material and Methods: In our study, we analyzed eleven patients diagnosed with MCC in our hospital between January 2010 and January 2020. Patients with perineural or vascular invasion, borderline microscopic positive findings, residual disease, and/or regional lymph node involvement among patients with tumors larger than 1.5 cm in pathology reports were referred to adjuvant treatment.

Results: The tumors were most frequently located in the thigh (25%), head-neck (25%), forearm (16.6%), inguinal (16.6%), and gluteal region (16.6%), respectively. The patients were followed up for an average of 38 months postoperatively (11-62 months). Complete cure was achieved in five (45.4%) of the cases. The average survival duration was 36 months (11-62 months). Recurrence was observed in two of our cases. Despite metastases occurring at different times in different abdominal organs abdomen, the surveillance was longer than expected, with an excellent response to multidisciplinary treatments.

Discussion: The features of the lesion should be carefully examined in the preoperative period. If in doubt, a sentinel biopsy should be performed during surgery by performing systemic screening. A multidisciplinary approach should be preferred in metastatic lesions. If intra-abdominal metastases are resectable, surgical treatment may prolong the surveillance.

Keywords

Merkel Cell Carcinoma, Metastasis, Surgical Treatment

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Introduction

Merkel cell carcinomas (MCC) are aggressive neuroendocrine tumors with the risk of local invasion, lymph node metastasis, and distant metastasis. It is approximately twice as mortal as malignant melanoma, a skin tumor with a poor prognosis. The 5-year survival has been reported to range between 0 and 18% for advanced-stage MCC [1]. Although its incidence according to geographical regions and races, it is common in the Caucasians and male gender in the age range of 70-80 [2,3]. Based on surveillance and epidemiology data in the United States, its current incidence was reported as 0.79 per 100,000. Caucasians account for 94.9% of these cases 1.0% are black, and 4.1% are other races (Asia-Pacific Islander, Native American, or other). These reports show that Merkel cell carcinoma is sporadic in patients of Asian descent [4].

For many years, the dissection of the primary tumor and regional lymph nodes with negative surgical margins subsequently adjuvant chemoradiotherapy (CRT) is the current treatment method for the treatment of MCC [5]. In our article, we evaluated 11 patients who were diagnosed with MCC between 2010 and 2020, who underwent surgical treatment solely, or received adjuvant chemoradiotherapy after surgical treatment. In one of our cases, which has not been encountered in the literature yet, gastric, testicular, and pancreatic metastases were encountered at different times during the course of the disease. Survival was prolonged with orchiectomy and pancreatectomy. This is the one and the only Merkel cell carcinoma case in the literature to have both pancreatic and gastric metastasis during the course of the disease. The demographic characteristics of the patients, tumor localization, treatment method, the existence of lymph node metastasis or distant metastasis, recurrences, and survivals were analyzed (Table 1). Our aim was to evaluate treatment modalities that can prolong survival in Merkel cell carcinoma.

Material and Methods

In our study, we analyzed 11 patients who were found to have Merkel cell carcinoma after 1862 surgical procedures performed under local anesthesia in our outpatient clinic conditions between January 2010 and January 2020. In these cases, the localization of the mass, its diameter, surgical margins, presence of re-excision, presence of distant metastases, presence of lymphatic dissection and survival were detailed. This study was approved by the Faculty of Medicine, Sakarya University Ethics Committee (No. 71522473/050.01.04/425; date: 27.07.2020). The National Comprehensive Cancer Network (NCCN) current guideline was used to determine the appropriate treatment method. Patients with perineural or vascular invasion, borderline microscopic positive findings, residual disease, and/or regional lymph node involvement among patients with tumors larger than 1.5 cm in pathology reports were referred to adjuvant treatment.

Descriptive analyses were performed to provide information on general characteristics of the study population. The Kolmogorov-Smirnov test was used to evaluate the normal distributions of numerical variables. Accordingly, the Mann-Whitney U test was used to compare the numeric variables between groups. The numeric variables were presented as mean \pm standard

deviation. Categorical variables were compared using the Chi-Square test. Categorical variables were presented as a count and percentage. A p-value <0.05 was considered significant. Analyses were performed using SPSS statistical software (IBM SPSS Statistics, Version 25.0. Armonk, NY: IBM Corp.)

Results

Seven of the twelve patients were male, five were female, and the average age was 73 years (50-88). The solitary lesion was detected in all patients. Tumors were most frequently located in the thigh (25%), head-neck (25%), forearm (16.6%), inguinal (16.6%), and gluteal region (16.6%), respectively. The patients were followed up for an average of 38 months postoperatively (11-62 months). Complete cure was achieved in five (45.4%) of the cases. Re-excision was performed in two patients due to positive surgical margins. Sentinel lymph node biopsy (SLNB) was performed in four patients. Lymph node dissection was performed due to detected lymph node metastasis in three of these patients. Distant metastases mainly were to bone and lung. The average survival duration was calculated 36 months (11-62 months). Recurrence was observed in two of our cases. Surgical treatment was applied to the 2.5 cm mass localized in the right gluteal area in a patient. Merkel cell carcinoma was revealed on the histological examination of the specimen, and surgical margins were clear (Figure 1A,1B, 1C). Right orchiectomy was performed when recurrence was detected in the right testicle on abdominal computed tomography (Figure 2A, 2B) of the patient who presented with complaint of testicular enlargement in the 12th month (Figure 1D, 1E). The patient received three cycles of cisplatin etoposide treatment. Distal pancreatectomy and splenectomy procedures were subsequently performed due to detected solitary metastasis in the distal pancreas on the abdominal tomography taken at 16 months (Figure 2C). Merkel cell carcinoma was revealed on the histological examination

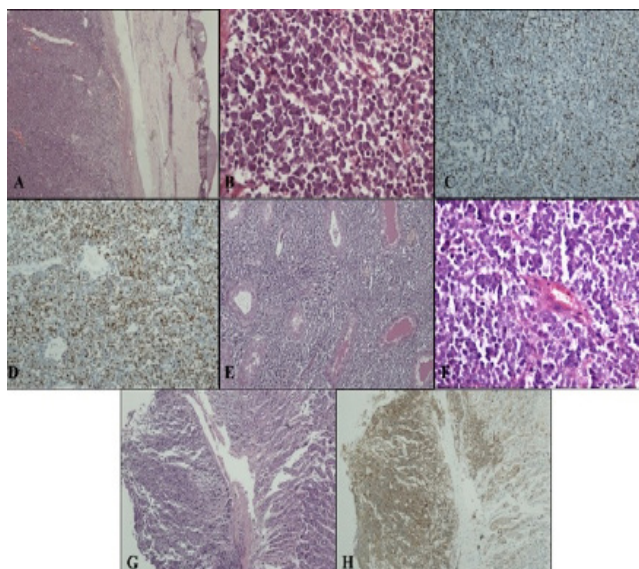


Figure 1. 1A-1B-1C: Histological examination of the MCC; 1D-1E : Histological examination of the MCC metastasis in the testicle; 1F: Histological examination of the MCC metastasis in pancreas and spleen; 1G-1H: Histological examination of the MCC metastasis on fundus and corpus of the stomach

Table 1. Demographic data of patients and clinical informations.

	Age	Site	Tumor on resection border/ Re- excision	Sentinel Lymph Node Biopsy	Lymph node dx	Metastasis	Cure	Survival (month)
1	56	Right cheek	Positive /Recurrence after 1 month	No	No	No	Yes	62
2	87	Left thigh	Negative	No	No	No	Yes	66
3	68	Right hand	Positive	No	No	Bone	(Exitus)	27
4	80	Left thigh	Negative	Yes	No	Sentinel Lymph Node Biopsy negative / Bone	No	18
5	88	Right forearm	Negative Recurrence in the same area after 4 years	No	No	No	Yes	53
6	75	Right preauricular	Positive/Re-excision	No	No	Bone/Lung	No	51
7	71	Left inguinal	Negative	Yes	Yes	Bone	No	44
8	50	Right gluteal	Positive	No	No	Testis (orchiectomy), Stomach, Pancreas (pancreatectomy)	(Exitus)	38
9	86	Left thigh	Negative	No	No	No	Yes	19
10	66	Left inguinal	Negative	Yes	Yes	No	No	12
11	70	Left gluteal	Negative	Yes	Yes	Lung	No	11

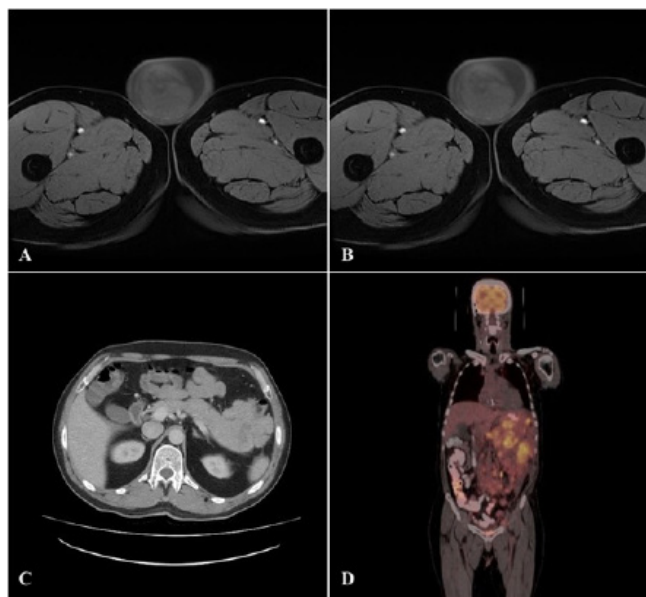


Figure 2. 2A-2B: Recurrence in the right testicle on abdominal computed tomography; 2C: Distal pancreatic metastasis of MCC on abdominal computed tomography; 2D: Widespread metastasis of MCC on positron emission tomography

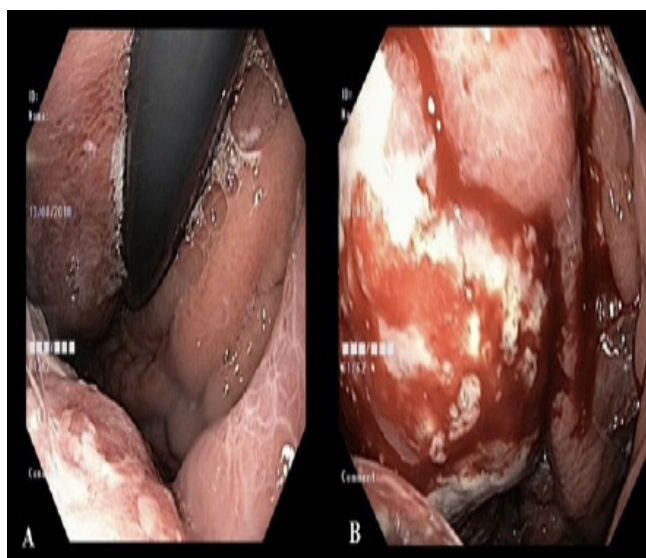


Figure 3. 3A-3B: MCC metastasis on fundus and corpus of the stomach in endoscopy

of the pancreas and spleen, and surgical margins were clear (Figure 1F). The patient, whose oncological treatment was continuing, was followed up in remission for 12 months. Merkel cell carcinoma metastasis was detected in biopsies taken from the mass found in the fundus and corpus of the stomach (Figure 3A, 3B) in the endoscopy performed upon the presence of epigastric pain at the 28th month of follow up (Figure 1G, 1H). The patient, who had widespread metastasis on control positron emission tomography (PET-CT) (Figure 2D), died in the 38th month of follow-up.

Despite metastases occurring at different times in different abdominal organs, the surveillance was longer than expected, with an excellent response to multidisciplinary treatments. Another feature of the case that has not yet been reported in the literature is the presence of gastric, pancreatic, and testicular metastases at different times.

Discussion

Although the clinical features of early-stage MCC are unclear, they may occur in erythematous, papillary, and nodular forms. It is usually diagnosed on the basis of histological and immunohistochemical findings. Most MCCs are seen in the head and neck site or extremities [6]. In our cases, tumors were frequently located in these sites. As a standard treatment option in early-stage MCC, local excision is performed considering the surgical margins [7]. In the case of suspicion, lymph node dissection may be considered if positive lymph nodes are detected on lymph node evaluation using Sentinel Lymph Node Biopsy (SLNB). In this case, the tumor stage is defined as stage 3. Adjuvant radiotherapy (RT) or re-excision may be considered if there are concerns about the surgical resection margin's adequacy for the primary tumor or the nodal staging process is missing [8]. According to the current NCCN guidelines, Stage II MCC standard treatment options include local excision with negative margins, followed by the SLNB procedure and adjuvant RT. Chemotherapy may be considered for patients with stage IV MCC, but there is insufficient evidence that chemotherapy results in permanent disease control or regional palliation [9]. According to recent NCCN guidelines, when clinically possible, local excision with a 1 or 2 cm intact margin should be performed in all primary MCC tumors [10]. However, different excision margins have not yet been compared in any controlled clinical

study [11]. In a large population study of primary MCC tumors by Perez et al, there was no significant association between the risk of local recurrence at the margin of 1 cm surgical resection and no significant effect in overall survival and disease-specific survival [12]. In our study, surgical resection with a 1 cm clear margin was performed in patients considered to have MCC before the surgical procedure. Male gender, advanced age, increased tumor size, and immunodeficiency have been associated with a poor prognosis in MCC [13]. However, lymph node involvement is the most important prognostic feature of clinically localized MCC [14, 15]. SLNB was performed in four patients who were thought to have lymph node involvement. Extended lymph node dissection was performed due to lymph node involvement detected in three of them. When the MCC patients presented to hospitals, their state was in 65% local disease, 26% regional lymph node metastasis, and distant metastasis in 8% [16]. MCC metastasizes most often to lymph nodes and then another skin area (9% -30%). These are followed by the lungs (10-23%), the central nervous system (18%), bone (10-15%), and the liver (13%). Lung and bone metastases were more common in our metastatic cases than in others. It is also possible to perform SLNB in patients with clinically negative lymph nodes, as roughly 20% to 30% of clinically negative MCC patients have positive SLN histology findings [17]. Since MCC is highly sensitive to radiation, adjuvant RT is an important component of MCC therapy. Even though Allen et al. [6] reported in a retrospective study that adjuvant RT could not provide significant local control, most of the other clinical studies showed that postoperative adjuvant RT improved local control to a greater extent [18,19]. Adjuvant RT is recommended for patients with a tumor larger than 1.5 cm who have vascular invasion, perineal invasion, positive microscopic margins on histopathological examination, residual disease, and/or regional lymph node involvement. According to NCCN guidelines, adjuvant nodal RT is routinely recommended when SLNB cannot be performed or when a patient presents clinically positive regional lymph node findings [10]. However, a more specific consensus is required on adjuvant RT indications. We applied postoperative radiotherapy to six patients with distant metastases. We also provided a complete cure with re-surgery for our patient who relapsed after four years in the same site. In a patient that suchlike a case has not existed in literature yet; We demonstrated that survival could be prolonged if synchronous resectable intra-abdominal and testicular metastases were surgically removed. MCC is a rare, aggressive skin cancer. Rapid diagnosis and active treatment are essential for the treatment of this disease. We recommend resection and subsequently postoperative RT in eligible patients with isolated intra-abdominal metastases, without peritonitis carcinomatosis. Further studies are needed with a high number of patients to conclude an accurate treatment strategy.

Conclusion

We demonstrated that survival could be prolonged if synchronous resectable intra-abdominal and testicular metastases were surgically removed. MCC is a rare, aggressive skin cancer. Rapid diagnosis and active treatment are essential for the treatment of this disease. We recommend resection

and subsequently postoperative RT in eligible patients with isolated intra-abdominal metastases, without peritonitis carcinomatosis. Further studies with a high number of patients are needed to conclude an accurate treatment strategy.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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